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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,296	07/28/2003	Lian-Chao Li	P06331US01	4176
27407	7590	04/04/2006	EXAMINER	
MCKEE, VOORHEES & SEASE, P.L.C. ATTN: PENNSYLVANIA STATE UNIVERSITY 801 GRAND AVENUE, SUITE 3200 DES MOINES, IA 50309-2721			KUMAR, VINOD	
		ART UNIT	PAPER NUMBER	
		1638		

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/628,296	LI ET AL.
	Examiner Vinod Kumar	Art Unit 1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 02 February 2006.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-5, 8-12 and 22-29 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 6,7 and 13-21 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 28 July 2003 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>02/09/2004</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED ACTION**

***Election/Restriction***

1. Applicant's election with traverse of Group IV, claims 6, 7 and 13-21 in the paper filed on February 2, 2006 is acknowledged. Applicant's arguments filed on February 2, 2006 have been fully considered but they are not persuasive. Applicant argue that that all Groups are related as products and methods limited to those products (response, page 7, last paragraph). The examiner maintains that restriction requirement is proper because literature search requires an extensive analysis of technical information divergent between Groups IV and I-III. Claims 6, 7 and 13-21 in conjunction with SEQ ID NO: 2 are examined in this Office action. Accordingly, claims 1-5, 8-12 and 22-29 and SEQ ID NOs. 8-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Non-elected subject matter must be removed from the elected claims. This restriction is made **FINAL**.

Elected Group IV comprises more than one amino acid sequence. Applicants are reminded that different amino acid sequences are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

**Applicants are required to elect** one amino acid sequence to be examined in conjunction with the elected Group of claims. In the instant case, one of SEQ ID NOs: 2, 8-17 or 18. This requirement is not to be construed as a requirement for an election

of species, since each nucleotide sequence is not a member of single genus of invention, but constitutes an independent and patentably distinct invention.

During a telephone conversation with Heidi Nebel on February 13, 2006 Applicants elected SEQ ID NO: 2 to be examined in conjunction with the elected Group IV claims (interview summary attached). Affirmation of this election must be made by applicant in replying to this Office action.

***Information Disclosure Statement***

2. An initialed and dated copy of Applicant's IDS form 1449 filed on February 9, 2004 is attached to the instant Office action.

***Specification***

3. The disclosure is objected to because of the following informalities:

The Figure 13 legend is objected to because it does not describe "related to amino acids". The brief description on figure should be amended to indicate that figure represents degeneracy of genetic code.

The abstract of disclosure is objected to because of the following informalities: Line 6 of Abstract recites "significant wall-loosening agent". This does not reflect claimed invention. It is suggested to insert --cell-- before "wall-loosening".

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1638

4. Claims 6, 7 and 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in their recitation "a group 2/3 allergen encoding a polypeptide", which is confusing, since it is unclear how an allergen can encode a polypeptide. Polypeptide is encoded by a nucleic acid or polynucleotide.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "a carboxy terminus", which is confusing, since it is unclear whether the polypeptide has more than one C-terminus. Further, what defines the carboxy terminus? Is it last 5 amino acids, the entire C-terminal half of the amino acid sequence or what?

Claims 6, 7 and 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "allergen", since it is unclear what the "allergen" comprises besides a polypeptide.

Appropriate corrections/clarifications are required.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 20 and 21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 20 and 21 read on a group 2/3 allergen per se, which is found in nature and thus, is unpatentable to applicant. The group 2/3 allergen, as claimed in claims 20 and 21, has the same characteristics as those found naturally or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brodgex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that claims 20 and 21 be amended by replacing the term "A" before "group 2/3 allergen" with --an isolated-- in line 1, to identify a product that is not found in nature.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 13-21 are rejected under 35 U.S.C. 112, first paragraph, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated group 2/3 allergen from grass pollen encoding a polypeptide as defined in SEQ ID NO: 2, does not reasonably provide enablement for any other group 2/3 allergen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims are broadly drawn to an isolated group 2/3 allergen encoding a polypeptide, or a group 2/3 allergen isolated from grass possessing expansin activity, or

an isolated group 2/3 allergen having expansin activity and more than one aromatic residue on its surface, or wherein group 2/3 allergen has the ability to enhance the wall loosening activity of a  $\beta$ -expansin in plant wall extension and stress relaxation activity, or wherein the enhancement is synergistic, or wherein said protein has wall loosening activity by itself, or wherein group 2/3 allergen is Lol p3, or a group 2/3 allergen that possesses expansin activity and is not affected by DTT, or a group 2/3 allergen having expansin activity and at least 40% sequence similarity to a carboxy terminus of a grass pollen 1 allergen.

Specification describes cloning of Lol p3 cDNA encoding a group 2/3 grass pollen allergen as defined in SEQ ID NO: 2 (Example 4, Page 34), and its expression in bacteria and subsequent purification of Lol p3 protein (Example 5, Page 35). The specification further describes expansin activity, cell wall extension and stress relaxation properties of said group 2/3 pollen allergen (Examples 6 and 7, Page 35-36).

Claims 13 and 14 encompass any group 2/3 grass pollen allergen having expansin activity and claims 15-21 encompass any group 2/3 allergen having expansin activity and the ability to enhance the wall-loosening activity of a  $\beta$ -expansin in plant wall extension and stress relaxation activity. Specification provides guidance on the isolation of Lol p3 pollen allergen encoding a protein (SEQ ID NO: 2) having expansin activity. The specification further provides guidance on the ability of Lol p3 pollen allergen to enhance the wall-loosening activity of  $\beta$ -expansin in plant wall extension and stress relaxation activity. However, specification provides no guidance on the isolation and expansin activity associated with large number of group 2/3 allergens from pollen or other tissues as encompassed by the claims. Specification also does not provide

guidance on the isolation and expansin activity of group 2/3 allergens from other organisms as encompassed by the claims.

Sampedro et al. (Genome Biology, 6:242.1-242.11) teach a grass group 2 pollen allergens (G2As) evolved from a truncated copy of a  $\beta$ -expansin gene with uncertain biological function. See Page 242.2, Paragraph 2. The claims encompass a group 2/3 allergen protein that may have similar structural characteristics, however, Keskin et al. (Protein Science, 13:1043-1055, 2004) teach that proteins with similar structure may have different functions. Besides, Thornton et al. (Nature structural Biology, structural genomics supplement, November 2000) teach that structural data may carry information about the biochemical function of the protein. Its biological role in the cell or organism is much more complex and actual experimentation is needed to elucidate actual biological function under *in vivo* conditions. While the specification teaches a *Lol p3* cDNA encoding SEQ ID NO: 2 (a group 2/3 allergen), it does not enable all cDNAs to encode for other group 2/3 allergen proteins. Undue experimentation by one skilled in art is required to isolate other group 2/3 allergen and use them in enhancing the cell-wall loosening activity of  $\beta$ -expansin in plant wall extension and stress relaxation activity. See In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 USPQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein. See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Thus, it is highly unpredictable that any group 2 /3 pollen allergen isolated from any organism will be associated with the same biological function as Lol p3 pollen allergen. Undue experimentation is required by a skilled artisan to isolate and use any group 2/3 allergen from any organism and use them in cell-wall loosening activity of  $\beta$ -expansin in plant wall extension and stress relaxation activity. See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification, as discussed above, undue experimentation would be required by one skilled in the art to make and use of claimed invention.

7. Claims 13-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are broadly drawn to a group 2/3 allergen encoding a polypeptide, or a group 2/3 allergen isolated from grass possessing expansin activity, or an isolated group 2/3 allergen having expansin activity and more than one aromatic residue on its surface, or wherein group 2/3 allergen has the ability to enhance the wall loosening activity of a  $\beta$ -expansin in plant wall extension and stress relaxation activity, or wherein the enhancement is synergistic, or wherein said protein has wall loosening activity by itself, or wherein group 2/3 allergen is Lol p3, or a group 2/3 allergen that possesses

expansin activity and is not affected by DTT, or a group 2/3 allergen having expansin activity and at least 40% sequence similarity to a carboxy terminus of a grass pollen 1 allergen.

Specification describes cloning of Lol p3 cDNA encoding a group 2/3 grass pollen allergen as defined in SEQ ID NO: 2 (Example 4, Page 34), and its expression in bacteria and subsequent purification of Lol p3 protein (Example 5, Page 35). The specification further describes expansin activity, wall extension and stress relaxation properties of said group 2/3 pollen allergen (Examples 6 and 7, Page 35-36).

Claims 13 and 14 encompass any group 2/3 grass pollen allergen having expansin activity and claims 15-21 encompass any group 2/3 allergen having expansin activity and the ability to enhance the wall-loosening activity of a  $\beta$ -expansin in plant wall extension and stress relaxation activity. All these claims described above encompass large number of unknown structures whose function has not been described in the specification. The specification describes just one structure of Lol p 3 cDNA encoding a polypeptide as defined in SEQ ID NO: 2 and further establishes its function in enhancing the wall-loosening activity of  $\beta$ -expansin in plant wall extension and stress relaxation activity. However, a group 2/3 allergen defined in SEQ ID NO: 2 does not represent the broadly claimed genus as encompassed by these claims. The claims encompass structures from different plant organs, plant species and other organisms whose function in cell wall-loosening activity has not been established. Furthermore, specification fails to describe the conserved domains that may be shared among the undisclosed structures, so that one skilled in the art can predictably determine the function of such structures similar to a 2/3 grass pollen allergen defined in SEQ ID NO:

2. Thus it is evident that Applicant never reduced their broadly claimed genus to practice.

Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide written description of the genus broadly claimed. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 6, 7 and 13-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ansari et al. (Biochemistry, 28:8665-8670, 1989) and evidenced by Marino et al. (Structure, 7:943-952, August 1999).

Claims are broadly drawn to a group 2/3 allergen encoding a polypeptide, or a group 2/3 allergen isolated from grass possessing expansin activity, or an isolated group 2/3 allergen having expansin activity and more than one aromatic residue on its surface, or wherein group 2/3 allergen has the ability to enhance the wall loosening

activity of a  $\beta$ -expansin in plant wall extension and stress relaxation activity, or wherein the enhancement is synergistic, or wherein said protein has wall loosening activity by itself, or wherein group 2/3 allergen is Lol p3, or a group 2/3 allergen that possesses expansin activity and is not affected by DTT, or a group 2/3 allergen having expansin activity and at least 40% sequence similarity to a carboxy terminus of a grass pollen 1 allergen.

Ansari et al. teach Rye Grass pollen allergen (a group 2/3 allergen) encoding a polypeptide which has 100% amino acid sequence identity to instant SEQ ID NO: 2, wherein N-terminal amino acid sequence of said polypeptide has sequence identity to instant SEQ ID NO: 15. The property of expansin activity is inherent to the amino acid sequence taught in the reference, as evidenced by the presence of expansin, cellulose-binding-like domain (PROSITE, Database of protein families and domains, Sequence Accession No. PS50843). The amino acid sequence taught in the reference comprises more than one aromatic amino acid residue. This is further evidenced by Marino et al. who teach the solution structure of Phl p 2 (a group 2/3 allergen) comprising at least more than one aromatic amino acid residue on the protein surface of said allergen. See Page 946, 2<sup>nd</sup> paragraph of column 2 and Figure 4; Page 948, Figure 5. The properties to enhance synergistically wall-loosening activity of a  $\beta$ -expansin in plant wall extension and stress relaxation activity is inherent to the group 2/3 allergen Lol p3 taught in the reference. The property of a group 2/3 allergen encoding a polypeptide that possesses expansin activity which is not affected by DTT is also inherent to the polypeptide taught in the reference as evidenced by the absence of cysteine residues in the amino acid sequence taught in the reference. Reference also teaches that Lol p II and Lol p III

(group 2/3 allergen) has at least 40% sequence similarity to a carboxy terminus of a grass pollen group I allergen. See Page 8665, Abstract and introduction; Page 8667, Figure 1; Page 8668, Figure 2; Page 8668, paragraph 1<sup>st</sup> of discussion.

### ***Conclusions***

9. Claims 6, 7 and 13-21 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



ASHWIN D. MEHTA, PH.D.  
PRIMARY EXAMINER